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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/786,926	GRALER ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22 and 27-36* is/are pending in the application.

4a) Of the above claim(s) *29,30 and 36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22,27,28 and 31-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *22 and 27-36* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendments of 11 December 2003, 03 October 2003, and 26 June 2003 have been entered in full. Claims 1-21 are cancelled. Claims 22-26 were added. Claim 22 is amended, claims 23-26 are cancelled, and claims 27-36 are added.

This application contains claims 29-30 and 36 drawn to an invention nonelected with traverse in the communication of (07 October 2002). A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 22, 27-28, and 31-35 are under consideration in the instant application.

Sequence Compliance

The Applicant's response to the Notice to Comply with Sequence Listing Requirements under 37 CFR §1.821 (11 December 2003) has been considered and is found persuasive. Therefore, the requirements set forth in the Notice to Comply (12 November 2003) are *withdrawn*.

Withdrawn Objections and/or Rejections

1. The objection to the specification for a lack of drawings at pg 3 of the previous Office Action (27 December 2002) is *withdrawn* in view of the submission of drawings (26 June 2003).

2. The objections to the specification at pg 3-4 of the previous Office Action (27 December 2002) are *withdrawn* in view of the amended abstract and title (26 June 2003).

3. The objections to claims 1 and 21 as set forth at pg 4 of the previous Office Action (27 December 2002) are *withdrawn* in view of the cancelled claims (26 June 2003).

4. The rejection of claims 1, 3-4, 12-13, and 21 under 35 U.S.C. § 101 for recitation of non-statutory subject matter as set forth at pg 4-5 of the previous Office Action (27 December 2002) is *withdrawn* in view of the cancelled claims (26 June 2003).

5. The rejection of claims 1, 3-4, and 21 under 35 U.S.C. § 101, as set forth at pg 5-8 of the previous Office Action (27 December 2002) is *withdrawn* in view of the cancelled claims (26 June 2003). Please see section on 35 U.S.C. § 101, below.

6. The rejection of claims 1, 3-4, and 21 under 35 U.S.C. § 112, first paragraph (enablement and written description) as set forth at pg 8-13 of the previous Office Action (27 December 2002) is *withdrawn* in view of the cancelled claims (26 June 2003). Please see section on 35 U.S.C. § 112, first paragraph, below.

7. The rejections of claims 1, 3-4, 12-13, and 21 under 35 U.S.C. § 112, second paragraph as set forth at pg 13-14 of the previous Office Action (27 December 2002) are *withdrawn* in view of the cancelled claims (26 June 2003). Please see section on 35 U.S.C. § 112, second paragraph, below.

8. The rejection of claims 1, 12, and 21 under 35 U.S.C. § 102(b) as set forth at pg 14-15 of the previous Office Action (27 December 2002) is *withdrawn* in view of the cancelled claims (26 June 2003).

New Claim Objections

9. Claim 28 is objected to because of the following informalities:

9a. In claim 28, line 3, the term "produce" should be amended to recite "product".

9b. Claims 27-28 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 27-28 do not further limit the claimed polynucleotide since they do not add any structural or functional language.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

10. Claims 22, 27-28, and 31-35 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Novel biological molecules lack well established utility and must undergo extensive experimentation. The basis for this rejection is set forth for cancelled claims 1, 3-4, and 21 at pg 5-8 of the previous Office Action (27 December 2002).

Claims 22 and 27-28 are directed to a kit comprising at least one diagnostic polynucleotide, wherein the diagnostic polynucleotide is selected from the group consisting of (a) a polynucleotide according to SEQ ID NO:2; (b) a polynucleotide that is at least 80% identical to SEQ ID NO: 2; (c) a polynucleotide encoding a GPCR having at least 82% sequence identity, or 91% sequence identity to the amino acid sequence of SEQ ID NO: 1; (c) a polynucleotide complementary to the polynucleotides of (a), (b), (c); a polynucleotide consisting of a portion of (a), (b), or (c). The claims also recite that the diagnostic polynucleotide is suitable for use as a probe or as a primer for performing PCR.

Applicant's arguments (26 June 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that the EDG6 receptor and its encoding DNA have been localized to various cells and tissues involved in immunity (pg 2, pg 4). Applicant argues that one of ordinary skill would appreciate the use of these probes for monitoring the local accumulation and/or proliferation of cells of the immune system. Applicant contends that determining the activity and infiltration of immune cells is relevant to several real world conditions (inflammation, leukemia, etc.) and is based on the specific distribution of EDG6 receptors. Applicant submits that at pg 7-8 of the non-final rejection, the Examiner has simply listed any possible utility and merely dismissed them out of hand. Applicant states that the PTO's Utility Examination Guidelines (January 7, 2003) indicate that "an assay which measures the presence of a material which has stated a correlation to a particular disease or condition" qualify as having a specific utility. Applicant argues that the Examiner has disregarded this procedural rule. Applicant also asserts that the specific experimentation, if necessary, is trivial and well within the capabilities of persons with ordinary skill. It is noted that Applicant cites the PTO Utility Examination Guidelines.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, although Applicant asserts that the EDG6 receptor and its encoding DNA have been localized to various cells and tissues involved in immunity, this asserted utility of cell/tissue typing is not specific or substantial. Such assays can be performed with any polynucleotide. The specification of the instant application does not disclose specific DNA sequences for use as markers for RFLP, to prepare primers, or to amplify DNA. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial. Furthermore, the asserted patentable utility of cell/tissue typing for the claimed EDG6 polynucleotide is not substantial because one skilled in the art would not readily

use the nucleotide sequences for tissue-typing in a real world sense since the DNA/protein is not specific to one tissue and is not associated with any disease or disorder (see pg 7-8). (In other words, the specification of the instant application does not indicate a correlation between the expression of the polynucleotide of SEQ ID NO: 2 and any specific disease or condition.) Furthermore, this asserted utility is not specific because numerous unrelated nucleotide sequences would also show a similar tissue typing pattern. Also, evidence of mere expression in a tissue is not tantamount to a showing of a role in any biological activity. Additionally, Applicant's asserted utility of using the DNA as probes for monitoring the local accumulation and/or proliferation of cells of the immune system is specific or substantial. Hybridization probes can be designed from any polynucleotide sequence. Further, the specification does not disclose specific cDNA, DNA, or RNA targets. The specification also discloses nothing about the type of expression indicative or not indicative of the accumulation and/or proliferation of cells of the immune system. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

It is clear from the instant specification that the "EDG6" protein described therein is what is termed an "orphan protein" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete characterization, this DNA and protein, may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent

in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to an isolated nucleic acid molecule comprising the nucleotide sequence set forth in SEQ ID NO: 2 which encodes a protein of as yet undetermined function or biological significance. Applicant asserts that the DNA of the instant specification and the protein encoded thereby are compounds which share structural and functional similarity to G protein-coupled receptors. However, the instant specification does not teach any significance or functional characteristics of the EGD6 GPCR polynucleotide (SEQ ID NO: 2) or polypeptide (SEQ ID NO: 1). The specification also does not disclose any methods or working examples that indicate the polynucleotide and polypeptide of the instant invention are involved in any activity. Since significant further research would be required of the skilled artisan to determine how the claimed polynucleotide and polypeptide is involved with an activity, the asserted utilities are not substantial. Additionally, G protein-coupled receptors (GPCRs) and signaling molecules are extremely diverse, as evidenced by Ji et al. (J Biol Chem 273(28):

17299-17302, 1998), and each new GPCR/signaling molecule needs to be evaluated empirically to determine the precise role(s) it plays.

Also, Applicant argues that the Examiner has simply listed any possible utility and merely dismissed them out of hand. However, the asserted utilities listed at pg 6-8 of the previous Office Action (27 December 2002), were disclosed in the instant specification (see pg 6 of previous Office Action for specific page numbers). The current rejection is in compliance with the most currently-published version of the Utility Guidelines which require that all biological inventions must have credible, specific and substantial ("real world") utility.

35 U.S.C. § 112, first paragraph

11. Claims 22, 27-28, and 31-35 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The basis for this rejection is set forth claims 1, 3-4, and 21 at pg 8 of the previous Office Action (27 December 2002).

12. Furthermore, claims 22, 27-28, and 31-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The basis for this rejection is set forth for claims 3 and 13 at pg 8-11 of the previous Office Action (27 December 2002).

Applicant's arguments (26 June 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that the drawings submitted 26 June 2003 better illustrate and clarify the extent to which the specification's guidance enables the claims. Applicant states that the specification provides a great deal of guidance as to making and using the claimed DNA, vectors, etc.

Applicant's arguments have been fully considered but are not found to be persuasive. It is noted that Applicant has not indicated where in the specification support can be located for making and using the claimed DNA, particularly fragments, variants, and mutants. The Examiner is also unable to find support. However, even if the specification discloses a broad brush discussion of making and screening for fragments, variants, and mutants, this discussion does not constitute a disclosure of a representative number of members. No such variants were made or shown to have activity. Only the EDG6 polynucleotide of SEQ ID NO: 2 and the polypeptide of SEQ ID NO: 1 are disclosed. The specification's general discussion of making and screening for variants would constitute an invitation to experiment by trial and error. Such trial and error experimentation is considered undue. The drawings filed in the specification also do not enable EDG6 or its fragments, variants, and mutants. As discussed in the previous Office Action (27 December 2002), certain positions in the amino acid sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions. However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in

these positions. Related literature, such as Spiegel (Annual Rev. Physiol. 58:143-170, 1995) and Pauwels et al. (Molec. Neurobiol. 17(1-3): 109-135, 1998) discuss gain-of-function and loss-of-function mutations in G protein-coupled receptors that cause a wide spectrum of hereditary and somatic disorders and diseases. For example, the ***single*** mutation of a lysine residue to a glutamate residue at position 296 in the rhodopsin receptor results in constitutive activation of that receptor and autosomal dominant retinitis pigmentosa (see Pauwels et al., pg 122, table 3). Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one or ordinary skill in the art to determine, without undue experimentation, the positions in the EDG6 protein and DNA which are tolerant to change and the nature and extent of changes that can be made in these positions.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to identify individuals or cells with a condition caused by a malfunctioning human EDG6 receptor or faulty EDG6 expression and to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to all of the above, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

13. Claims 22, 27-28, and 31-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 22, 27-28, and 31-25 are directed to a kit comprising at least one diagnostic polynucleotide, wherein the diagnostic polynucleotide is selected from the group consisting of (a) a polynucleotide according to SEQ ID NO:2; (b) a polynucleotide that is at least 80% identical to SEQ ID NO: 2; (c) a polynucleotide encoding a GPCR having at least 82% sequence identity, or 91% sequence identity to the amino acid sequence of SEQ ID NO: 1; (c) a polynucleotide complementary to the polynucleotides of (a), (b), (c); a polynucleotide consisting of a portion of (a), (b), or (c). The claims also recite that the diagnostic polynucleotide is suitable for use as a probe or as a primer for performing PCR. The claims recite a vector suitable for cloning and gene transfer.

The specification of the instant application teaches that "in diseases caused by expression deviating from the norm or by receptor mutation, diagnostics can be done, e.g. with test kits on the basis on monoclonal antibodies or nucleic acid proof processes" (pg 5, lines 13-16). However, the specification does not disclose a correlation between a specific disease state and an alteration in expression level, form, temporal pattern, etc. of the EDG6 nucleic acid sequence of SEQ ID NO: 2. Significant further experimentation would be required of the skilled artisan to identify individuals with a disease involving the EDG6 nucleic acid molecule of SEQ ID NO: 2 or its variants. (Note, this issue could be overcome by deleting the word "diagnostic" from the claims.)

Furthermore, the Examiner has interpreted "a vector suitable for cloning and gene transfer" in claims 31-35 as reading upon the generation of transgenics, gene therapy, and/or animal cloning. There are no limitations in the claims regarding the type of cloning or gene

transfer encompassed. The specification of the instant application does not teach any methods or working examples that indicate an EDG6 polynucleotide is introduced and expressed in any cell, particularly that of a multicellular organism. There are also no methods or working examples in the specification indicating that any organisms are cloned. The specification does not teach how to use an EDG6 polynucleotide without undue experimentation for the treatment of a disease in an animal. There are no working examples directed to a particular disorder in an animal or administration of any EDG6 polynucleotide to an animal for treatment. Relevant literature teaches that since 1990, about 3500 patients have been treated via gene therapy and although some evidence of gene transfer has been seen, it has generally been inadequate for a meaningful clinical response (Phillips, A., J Pharm Pharmacology 53: 1169-1174, 2001; abstract). Additionally, the major challenge to gene therapy is to deliver DNA to the target tissues and to transport it to the cell nucleus to enable the required protein to be expressed (Phillips, A.; pg 1170, ¶ 1). Phillips also states that the problem with gene therapy is two-fold: 1) a system must designed to deliver DNA to a specific target and to prevent degradation within the body, and 2) an expression system must be built into the DNA construct to allow the target cell to express the protein at therapeutic levels for the desired length of time (pg 1170, ¶ 1). Therefore, undue experimentation would be required of the skilled artisan to introduce and express an EDG6 nucleic acid into the cell of an organism. Undue experimentation would also be required of the skilled artisan to clone an animal. Additionally, it is unpredictable and complex wherein one skilled in the art may not necessarily be able to introduce and express an EDG6 nucleic acid in the cell of an organism or be able to produce an EDG6 protein in that cell.

Due to the large quantity of experimentation necessary to determine a correlation in a specific disease with the EDG6 nucleic acid sequence of SEQ ID NO: 2 and to determine the

quantity of EDG6 polynucleotide to be administered, the most effective administration route, and the duration of the treatment, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the EDG6 polynucleotide *in vivo* and the unpredictability of identifying individuals with a disease involving EDG6, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Written Description

14. Claims 22, 27-28, and 31-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is set forth for claims 3 and 13 at pg 11-13 of the previous Office Action (27 December 2002).

The claims are directed to a kit comprising at least one diagnostic polynucleotide, wherein the diagnostic polynucleotide is selected from the group consisting of a polynucleotide that is at least 80% identical to SEQ ID NO: 2; a polynucleotide encoding a GPCR having at least 82% sequence identity, or 91% sequence identity to the amino acid sequence of SEQ ID NO: 1; a polynucleotide complementary to the polynucleotides of above; a polynucleotide consisting of a portion of the above polynucleotides.

Applicant's arguments (26 June 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that the sequence described by the mouse receptor of SEQ ID NO: 4 is 82% identical to the human/wild type protein. Applicant argues that SEQ ID NO: 4 can be thought of as an actual mutant/variant of the human receptor. Applicant contends that the comparison of these two proteins would provide a great deal of information about the proteins' structure-function relationships.

Applicant's arguments have been fully considered but are not found to be persuasive. Applicant's arguments have been fully considered but are not found to be persuasive because the Applicant has not provided evidence to demonstrate that the skilled artisan would be able to envision the detailed structure of the infinite number of polynucleotides recited in the claims. The description of one EDG6 polynucleotide and polypeptide in the specification of the instant application is not a representative number of embodiments to support the description of an entire genus of functionally equivalent polynucleotides and polypeptides which incorporate all mutants, derivatives, variants and fragments. Therefore, only an isolated nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO: 2 and a nucleic acid molecule which encodes a polypeptide consisting of the amino acid sequence of SEQ ID NO: 1, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

Furthermore, to provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a partial structure in the form of a recitation of percent identity and polynucleotide/polypeptide fragments. There is not even identification of any particular portion

of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

New Matter

15. Claims 22, 27-28, and 31-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a kit comprising at least one diagnostic polynucleotide, wherein the diagnostic polynucleotide is selected from the group consisting of (a) a polynucleotide according to SEQ ID NO:2; (b) a polynucleotide that is at least 80% identical to SEQ ID NO: 2; (c) a polynucleotide encoding a GPCR having at least 82% sequence identity, or 91% sequence identity to the amino acid sequence of SEQ ID NO: 1; (c) a polynucleotide complementary to the polynucleotides of (a), (b), (c); a polynucleotide consisting of a portion of (a), (b), or (c). The claims also recite that the diagnostic polynucleotide is suitable for use as a probe or as a primer for performing PCR. Additionally, the claims disclose a vector and bacterial cells and mammalian cells comprising the vector.

The specification as originally filed does not provide adequate written description for : ***(1)*** a polynucleotide that is at least 80% identical to the polynucleotide of SEQ ID NO: 2; ***(2)*** a polynucleotide complementary to the polynucleotides of (a), (b), (c); ***(3)*** a polynucleotide consisting of a portion of the polynucleotides of (a), (b), (c); ***(4)*** detecting the presence of leukocytes and lymphoid cells in a tissue or cell sample; ***(5)*** a vector suitable for cloning and

gene transfer; ***(6)*** the polynucleotide is suitable for use as a probe in blotting assays, wherein hybridization of the probe to immobilized nucleic acid sequences obtained from a tissue- or cell-sample is indicative of the presence of leuckocytes or lymphoid cells in the sample; ***(7)*** the polynucleotide is suitable as a primer for performing PCR on the tissue- or cell-sample's RNA or DNA, and wherein the produce of said PCR is indicative of the presence of leukocytes or lymphoid cells in the sample; ***(8)*** a eukaryotic viral promoter; ***(9)*** a vector comprising a promoter operably linked to the claimed polynucleotide and wherein the promoter effectively provides for the expression of the polynucleotide in a mammalian host cell; ***(10)*** a bacterial cell comprising a vector; and ***(11)*** a mammalian cell comprising a vector. These are not expressly asserted, nor do they flow naturally from the specification.

35 USC § 112, second paragraph

16. Claims 22, 27-28, and 31-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

17. Claims 22, 27-28, and 31-35 are rejected as being indefinite because it is unclear whether open or closed term language is intended in claims 22(a) and 31(a). See MPEP § 2111.03.

18. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely

exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim s 22, 27-28, and 31-35, particularly claims 22(c) and 31(c) recite the broad recitation "having at least 82% sequence identity to", and the claim also recites "or, 91% sequence similarity with" which is the narrower statement of the range/limitation.

19. Claims 33-34 are rejected as being indefinite because "mammalian cell" in claims 33-34 is a relative term which renders the claims indefinite. For example, it cannot be determined if the mammalian cell is isolated or if the cell is from a multicellular transgenic animal. (Please note that this issue could be overcome by amending the claims to recite, for example, "An isolated mammalian cell...".)

20. Claims 22, 27-28, and 31-35 are rejected as being indefinite because the elements recited in claim 22(a)-22(e) and claim 31(a)-31(e) do not constitute proper Markush groups. See MPEP § 2173.05(h).

21. The term "cloning" in claims 31-35 is a relative term which renders the claims indefinite. The term "cloning" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It cannot be determined what type of cloning is encompassed by the claim. For example, reproducing DNA or cloning in an animal?

22. The term "gene transfer" in claims 31-35 is a relative term which renders the claims indefinite. The term "gene transfer" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would

not be reasonably apprised of the scope of the invention. It cannot be determined what type of gene transfer is encompassed by the claim. For example, gene transfer into an isolated host cell or to create a transgenic organism? Gene therapy?

Claim Rejections - 35 USC § 102

23. Claims 22 and 27-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Graler et al. (Genomics 53(2): 164-169, 1998). It is noted to Applicant that since the claimed human EDG6 polynucleotide of SEQ ID NO: 2 and the polypeptide of SEQ ID NO: 1 have no utility under 35 U.S.C. §101, first paragraph, the effective filing date of the instant application is May 4, 2001. The basis for this rejection is set forth for claims 3-4 and 12 at pg 14-16 of the previous Office Action (27 December 2002).

Applicant's arguments (26 June 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant argues that the previous claims have been canceled. They have been replaced by new claims and therefore, this rejection is overcome.

Applicant's arguments have been fully considered but are not found to be persuasive. As discussed in the previous Office Action, Graler et al. teaches the DNA sequence coding the human G-protein coupled receptor EDG6. Graler et al. also discloses the nucleic acid sequence of SEQ ID NO: 2 of the instant application. (See sequence alignment attached to the previous Office Action as Appendix B; see nucleotides 1-1155 of the instant application; see also nucleotides 23-1177 of Graler et al.)

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BEB
Art Unit 1647
12 July 2004

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